

Peri-extubation practices and extubation failure in a South African tertiary paediatric intensive care unit

Marie-Charlyne Fatima Kilba

Student number: KLBMAR004

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Supervisors:

1. Dr. Shamiel Salie

Department of Paediatrics and Child Health, University of Cape Town
Red Cross Children's Hospital, Paediatric Intensive Care Unit

2. Prof. Brenda Morrow

Department of Paediatrics and Child Health, University of Cape Town
Red Cross Children's Hospital, Paediatric Intensive Care Unit

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DECLARATION

I, Marie-Charlyne Fatima Kilba, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Signed by candidate

Date: 27/01/2019

Thesis abstract

Objectives

To describe the peri-extubation practices in a South African paediatric intensive care unit and to determine the prevalence, risk factors and outcomes of extubation failure.

Design

Prospective observational study.

Setting

A multi-disciplinary paediatric intensive care unit in Cape Town, South Africa.

Patients

All intubated and ventilated patients between May and September 2017.

Interventions

There were no research- related interventions

Measurements and Main Results

Extubation failure was defined as requiring re-intubation within 48 hours of planned extubation. Two hundred and sixteen intubations in 204 children, with a median age of 8 months (IQR 1.6 – 44.4) and median PIM3 risk of mortality score 0.03 (IQR 0.01 – 0.07) were included. There were 184 planned extubations; 21 (10.3%) patients died before extubation; two (1%) had tracheostomies; two (1%) were transferred intubated and seven (3.4%) had ventilation withdrawn. Non-invasive ventilation was implemented in 97 cases (52.7%) after planned extubation.

There were 21 (11.4%) failed extubations. Indications for re-intubation were: upper airway obstruction (n=7; 33.3%); respiratory failure (n=4; 19.0%); heart failure (n=3; 14.3%); diaphragm paralysis, hypoventilation and cardiac arrest (n=2; 9.5% each); and reduced level of consciousness (n=1; 4.8%).

Prematurity (adjusted OR 1.8 (95% CI 0.05 – 0.6); p =0.004), dysmorphology (OR 1.8 (95% CI 0.05 – 0.6); p=0.022), decreased level of consciousness (OR 4.8 (95% CI 1.96 – 11.7); p=0.001) and ventilation \geq 48 hours (OR 0.2 (95% CI 0.05 – 0.7); p = 0.003) were independently associated with extubation failure on multivariate analysis.

Children who failed extubation had longer duration of ventilation (median 231 versus 53 hours; $p < 0.0001$), PICU length of stay (median 15 versus 5 days; $p < 0.0001$) and hospital length of stay (32 versus 15 days; $p=0.009$); and higher mortality (28.6% versus 6.7%; $p = 0.001$) compared to those successfully extubated.

Conclusion

Extubation failure is associated with significant morbidity and mortality. Independent risk factors of extubation failure identified in our context were prematurity, dysmorphology, impaired consciousness and ventilation for more than 48 hours.

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Abbreviations

BiPAP	bi-level positive airway pressure
CPAP	continuous positive airway pressure
CPIS	clinical pulmonary infection score
ETT	endotracheal tube
FiO ₂	fraction of inspired oxygen
HFNC	high flow nasal cannula
IQR	interquartile range
NIV	non-invasive ventilation
OR	odds ratio
pCO ₂	partial pressure of carbon dioxide
PICU	paediatric intensive care unit
PIM3	paediatric index of mortality 3
pO ₂	partial pressure of oxygen
SBT	spontaneous breathing trial
VAP	ventilator associated pneumonia
WHO	world health organization

Chapter 1: Introduction

1.1 Context

Mechanical ventilation is a life- saving intervention that has evolved greatly since the first negative pressure ventilation tanks used in the 1920's polio epidemic (1). Mechanical ventilation can be delivered invasively through an endotracheal tube (ETT) or a tracheostomy tube, or noninvasively through an interface such as nasal prongs or mask, facemask, or a helmet. Various modes of ventilation have been developed and the choice of which mode to use depends, amongst others, on the patient's disease and comorbid factors, (2) and the clinicians preference.

Indications for mechanical ventilation

The proportion of children mechanically ventilated in paediatric intensive care units (PICUs) ranges from 20% to over 60% in different settings (3-6). The primary indication for assisted ventilation is respiratory failure (2). This may be a result of primary airway or lung disease, or secondary to other organ or system failures, example cardiovascular disease, neurologic and neuromuscular disorders (7). Pneumonia accounts for one in six deaths in children under 5 years of age world wide with most of the deaths occurring in low and middle income countries (9). Despite the decreasing overall under 5 mortality rates, the decrease in pneumonia-related deaths lags behind (9). The situation in South Africa is similar to the global picture and pneumonia remains a major cause of morbidity and mortality (10)

In a secondary analysis of a multicentre study carried out across 16 PICUs in the United States to screen for acute lung injury, the characteristics of intubated and ventilated children were analysed. Thirty percent of all PICU admissions were intubated and ventilated with individual centre ranges between 20-64%. Of these, 46% were ventilated for respiratory disease; 30% for cardiac disease; 9% for spinal and neuromuscular disease and 2.4% for cerebral hypertension (4). A similar single site two- year retrospective study at the Aga Khan University Hospital's PICU in Pakistan reported that 50.7% of admissions required

mechanical ventilation. Of these, 35.8% were for neurological illnesses; 20.8% for respiratory disease and 13% for cardiac disease (5). At the Red Cross War Memorial Children's Hospital in Cape Town, approximately 50% of children admitted to the PICU were invasively mechanically ventilated in 2009 (11). Over the past few years the use of non-invasive ventilatory support has increased and as such, may have led to a decrease in the need for invasive ventilation.

Adverse events associated with invasive mechanical ventilation

Mechanical ventilation is not without risks and could result in added morbidity and mortality. Adverse events include:

- Injury to the airway from the ETT and associated endotracheal suction manoeuvres and devices (12, 13)
- Volume and pressure-related lung injury (volutrauma/barotrauma) that also causes release of inflammatory mediators which worsen lung injury and cause additional distant organ injury (14)
- Atelectasis (15)
- Diaphragmatic dysfunction (16)
- Impaired cardiac output secondary to heart-lung interaction (17)
- Ventilator associated infections (18)
- Invasive ventilation may also require increased levels of analgesia and sedation to prevent ventilator-patient dyssynchrony, minimize self-injury and prevent unplanned extubation (2, 19). Sedatives however, may also increase the risk of extubation failure or result in delirium and withdrawal symptoms (20).

The risk of complications increases with duration of ventilation. It is therefore important to wean ventilation as the child improves and extubate once the child is able to sustain adequate spontaneous respiration. Extubation failure and re-intubation is associated with increased morbidity, length of PICU stay and cost, and mortality (21-23). As such it is important that extubation is neither rushed nor prolonged unnecessarily.

Weaning and assessment of extubation readiness in children

Institutional weaning protocols have been shown to help shorten the duration of weaning and ventilation in some adult studies (24) but have not been documented to significantly change outcomes such as length of PICU stay or mortality in children. A multicentre randomised controlled trial on the effect of mechanical ventilation weaning protocols on respiratory outcomes in infants and children found weaning periods generally to be short, with no significant difference in weaning duration and extubation failure between those in the weaning protocol group and those in the non-protocol group (25).

Prediction of extubation outcome is difficult because several factors are necessary for effective spontaneous breathing. These include adequate respiratory drive, effective airway reflexes and clearance, respiratory muscle strength and load, effective gas exchange and ventilation-perfusion match (26).

It is estimated that between 25-40% of extubation failures are as a result of upper airway obstruction. The endotracheal cuff leak test was developed to help predict laryngeal oedema. However, this is difficult to reproduce and has a low positive predictive value for post extubation stridor (27, 28).

Objective weaning and extubation readiness tests therefore remain elusive in paediatric practice and depend largely on the clinical judgment of the attending physician (29).

Extubation failure

Extubation is the act of removal of an endotracheal tube. Extubation failure is defined as the need for re-intubation within hours or days of a planned extubation.

Various studies have used different time frames in the definition of extubation failure, ranging from 24 to 72 hours, even up to seven days (30), making comparison of prevalence challenging. For this study, requiring re-intubation

within 48 hours was considered a failed extubation based on the definition used by the Pediatric Cardiac Critical Care Consortium (31). Extubation failure, requiring re-intubation within 48 hours of a planned extubation, has been reported to range between four and 20% (31) (32) (5).

Risk factors for extubation failure

A number of factors have been associated with increased risk of extubation failure. These include; mechanical ventilation for more than 24 hours, age less than 24 months, airway abnormalities, syndromes, chronic neurologic or respiratory disease, cardiac disorders, positive fluid balance and malnutrition (4, 21, 33, 34).

Upper airway obstruction (UAO) accounts for 25-40% of extubation failure (28, 35). It may be as a result of laryngeal, subglottic or supraglottic oedema, granulomas or vocal cord paralysis.

The prophylactic use of corticosteroids for the prevention of post extubation stridor and extubation failure remains controversial. A Cochrane review of studies involving neonates, children and adults showed a general non significant decrease in stridor and extubation failure with administration of steroids, but a significant reduction in the incidence of post extubation stridor and extubation failure in children with underlying airway abnormalities (36). This suggests that targeted use in those at risk of UAO is beneficial.

Non-invasive ventilation (NIV) after extubation

The use of NIV in the management of acute respiratory failure in both children and adults has increased in recent years, reducing the need for invasive mechanical ventilation (37, 38). NIV has also been used to facilitate weaning and prevent re-intubation after invasive mechanical ventilation. Success rates with post extubation NIV use in paediatric studies range between 65-85%. Outcomes

were better in those who received NIV immediately after extubation than in those in whom NIV was started later for post-extubation respiratory failure (38-40).

Rational for study

Extubation failure is associated with significant adverse outcomes including increased mortality, prolonged PICU and hospital stay, higher costs, and greater need for tracheotomy (30) (22) (21). There is a paucity of data on peri-extubation practices and extubation failure in Africa generally and especially among children.

Extubation failure rates and outcomes had not been systematically documented in our PICU, but unpublished data from a study on the outcomes of cardiac patients admitted to the unit showed an extubation failure rate of 5.7% among elective cardiac admissions and 13% among emergency cardiac admissions. The prevalence of extubation failure in other patient groups (e.g. emergency medical admissions, neurosurgery/neurology and general surgery) admitted to this multi-disciplinary PICU was unknown.

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1.2 Ethical considerations

Approval for the study was obtained from the following before commencing with data collection:

1. Department of Paediatrics Research Committee (DRC)
2. University of Cape Town's Faculty of Health Sciences Human Research Ethics Committee (HREC); HREC Ref: 166/2017
3. Medical superintendent of Red Cross War Memorial Children's Hospital.

A waiver of consent was granted by the HREC.

The study adhered to the requirements laid out in the Declaration of Helsinki 2013.

1.3 Instructions to authors for publication- ready manuscript

Chapter 2 (publication-ready manuscript) conforms to the author guidelines (Appendix 5) for submission to *Pediatric Critical Care Medicine*, an international peer reviewed and PubMed accredited journal with impact factor 2.326.

CHAPTER 2 – Publication-ready manuscript

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Title Page

Title: Peri-extubation practices and extubation failure in a South African tertiary paediatric intensive care unit

Authors: Kilba, MC^{1,2}; Salie, S^{1,2}; Morrow, BM^{1,2}

1. Department of Paediatrics, University of Cape Town
2. Paediatric intensive care unit, Red Cross War Memorial Children's Hospital

Corresponding author details:

Marie-Charlyne F. Kilba
Red Cross War Memorial Children's Hospital
2nd Floor R00219 ICH Building,
Klipfontein Rd, Rondebosch
7700, Cape Town, South Africa

Charlyne.kilba@gmail.com
+233 206301131

Keywords: intubation; extubation failure; risk factors; paediatric intensive care unit; mechanical ventilation; outcomes

Abstract

Objectives: To describe the peri-extubation practices in a South African paediatric intensive care unit and to determine the prevalence, risk factors and outcomes of extubation failure.

Design: Prospective, observational study

Setting: Multi-disciplinary PICU in Cape Town, South Africa

Patients: All intubated and ventilated patients between May - September 2017.

Interventions: There were no research- related interventions

Measurements and Main Results: Extubation failure was defined as requiring re-intubation within 48 hours of planned extubation. Two hundred and sixteen intubations in 204 children with a median age of 8 months (IQR 1.6 – 44.4) and median PIM3 risk of mortality score 0.03 (IQR 0.01 – 0.07) were included. There were 184 planned extubations; 21 (10.3%) patients died before extubation; two (1%) had tracheostomies; two (1%) were transferred intubated and seven (3.4%) had ventilation withdrawn. Non-invasive ventilation (NIV) was implemented in 97 cases (52.7%) after planned extubation.

There were 21 (11.4%) failed extubations. Indications for re-intubation were: upper airway obstruction (n=7; 33.3%); respiratory failure (n=4; 19.0%); heart failure (n=3; 14.3%); diaphragm paralysis, hypoventilation and cardiac arrest (n=2; 9.5% each); and reduced level of consciousness (n=1; 4.8%).

Prematurity (adjusted OR 1.8 (95% CI 0.05 – 0.6); $p=0.004$), dysmorphology (OR 1.8 (95% CI 0.05 – 0.6); $p=0.022$), decreased level of consciousness (OR 4.8 (95% CI 1.96 – 11.7); $p=0.001$) and ventilation ≥ 48 hours (OR 0.2 (95% CI 0.05 – 0.7); $p=0.003$) were independently associated with extubation failure on multivariate analysis.

Children who failed extubation had longer duration of ventilation (median 231 versus 53 hours; $p<0.0001$), PICU length of stay (median 15 versus 5 days; $p<0.0001$) and hospital length of stay (32 versus 15 days; $p=0.009$); and higher mortality (28.57% versus 6.75%; $p=0.001$) compared to those successfully extubated.

Conclusion: Extubation failure is associated with significant morbidity and mortality. Independent predictors of extubation failure in our context were identified.

Introduction

The proportion of children mechanically ventilated in paediatric intensive care units (PICU's) ranges from 20% to over 60% in many settings (1-4). The primary indication for assisted ventilation is respiratory failure which may be a result of primary airway or lung disease, or secondary to other organ failures, or for postoperative care (5).

The risk of morbidity and mortality increases with the duration of mechanical ventilation. Extubation failure is also associated with significant adverse outcomes including increased mortality, prolonged PICU and hospital stay, higher costs, and greater need for tracheotomy (6-8) (9). As such it is important that extubation is neither rushed nor unnecessarily prolonged.

Prediction of extubation readiness and outcome is difficult as several factors are necessary for effective spontaneous breathing. These include adequate respiratory drive, patent airways, effective airway reflexes and clearance, adequate respiratory muscle strength, effective gas exchange, ventilation-perfusion matching and haemodynamic stability (10).

Weaning protocols have not always been found to shorten duration of ventilation significantly in the paediatric population (4, 11, 12), and are more challenging in young children (12). There are also no reliable methods for assessing readiness for and predicting extubation outcome in children. Indices such as the Rapid Shallow Breathing Index (RSBI), Compliance, Resistance, Oxygenation, Pressure index (CROP index), negative inspiratory pressure, and volumetric capnography are less reliable in children compared to adult studies.(13-16). In addition, the cuff leak test has a low positive predictive value for post extubation upper airway obstruction, which is one of the commonest reasons for re-intubation in children (17-19). Objective weaning and extubation readiness tests therefore remain elusive in paediatric practice and depend largely on the clinical judgment of the attending physician (13).

The use of non-invasive ventilation (NIV) in the management of acute respiratory failure in both children and adults has increased in recent years reducing the need for invasive mechanical ventilation (20, 21). It has also been used to facilitate weaning and prevent re-intubation after invasive mechanical ventilation. Success rates with post extubation NIV use in paediatric studies range between 65-85%. Outcomes were better in those who received NIV immediately after extubation than in those in whom NIV was started later for post-extubation respiratory failure (21-23).

There is a paucity of data on the outcomes of African children requiring mechanical ventilation, the risk factors for extubation failure and extubation failure rates. This study therefore aimed to document the extubation failure rate, the risk factors and outcomes of failed extubation, and the outcome of the use of NIV post extubation in children mechanically ventilated in the PICU of Red Cross War Memorial Children's Hospital, Cape Town, South Africa.

1.1 Materials and methods

1.1.1 Population

All children intubated during their admission to the PICU from 15th May to 15th September 2017, including those who were intubated outside the PICU.

Exclusion criteria

1. Children admitted to the PICU with a tracheostomy or admitted for a planned tracheostomy.
2. Children who were brain dead and were admitted to the PICU for the sole purpose of organ donation.
3. Children extubated as part of a palliative care plan were excluded from the extubation failure analyses.

1.1.2 Study site

The study site was the PICU of Red Cross War Memorial Children's Hospital; a 22-bedded multidisciplinary unit situated in a tertiary paediatric hospital in Cape Town, South Africa. The PICU admits approximately 1,300 patients per annum with a mortality rate of 6%. Admissions are mainly for the management of infectious diseases such as pneumonia and sepsis, trauma and post cardiac surgery care.

1.1.3 Methods

In our PICU, the decision to extubate, administer steroids prior to extubation and the elective use of NIV after extubation are made by the attending physician, based mainly on clinical parameters.

There were no weaning protocols and standardized spontaneous breathing trials (SBT) were not carried out.

The study was a prospective observational study, over a four-month period from 15th May to 15th September 2017.

Participants were recruited into the study at the time of decision to extubate and peri-extubation data filled into a standardized case record form by the doctor who carried out the extubation.

Intubation data was captured from the PICU intubation checklist (Appendix 2), which was completed at the time of intubation by the doctor who carried out the procedure. For intubations that occurred outside the PICU, the data was extracted from the clinical notes. The appropriateness of the ETT internal diameter used was assessed with the $(\text{Age}/4) + 4$ formula for children one year and above for uncuffed tubes, and $(\text{Age}/4) + 3.5$ mm for cuffed tubes. For the infants, the weight-based recommendation from the Textbook of Neonatal Resuscitation (7th edition) was used. Mallinckrodt cuffless and Parker ThinCuff

microcuff tubes were used for intubations carried out in the PICU. The bedside nurse routinely checked cuff pressures.

Remaining data were extracted from the patients' clinical notes, medication and observation charts. If a child needed to be re-intubated, the attending doctor filled in the re-intubation data. Extubation failure was defined as requiring re-intubation within 48 hours of a planned extubation (9). The level of consciousness was scored using the Alert Verbal Painful Unresponsive (AVPU) scale.

Since this study aimed to describe the current practice in the PICU, diagnosis and classifications were recorded as stated in patient notes. The diagnosis of ventilator-associated pneumonia (VAP) was made, as per standard practice, based on the modified clinical pulmonary infection score (CPIS)(24) (25) which were documented daily by the attending doctor. In addition, the infection prevention and control (IPC) surveillance team routinely audited the CPIS forms to diagnose or exclude VAPs using the same criteria. The predicted mortality risk, using the Paediatric Index of Mortality 3 (PIM3) was obtained from the PICU admissions database. Children discharged on NIV were followed up on the ward to document the duration of use and complications.

The outcome at 30 days post PICU discharge was obtained from the hospital database and patient notes.

1.1.4 Data management and Analysis

Data collected using standardized, self-developed case record forms were entered into an SPSS spreadsheet and analysed using SPSS and Statistica version 13 (Statsoft Inc, USA). The data were tested for normality using the Kolmogorov-Smirnov test and presented mainly as median (IQR) as majority of the data were not normally distributed. Comparisons of patient characteristics with and without extubation failure were analysed using Chi² tests for categorical variables and Mann-Whitney U tests for continuous variables. Variables found to

be significantly associated with the primary outcome of extubation failure on univariate analysis, were entered into a backward stepwise regression model, in order to determine independent associations with the primary binary outcome. A significance level of 0.05 was chosen.

Results

There were 446 admissions during the study period and 216 (48.43%) of them were invasively ventilated. Two hundred and sixteen episodes of mechanical ventilation in 204 children were captured. There were 104 (48.1%) males; median age of 8 months (IQR 1.6 – 44.4) and median PIM3 risk of mortality score 0.03 (IQR 0.01 – 0.07). Four children were intubated and ventilated twice during a single admission but did not fail their first extubation. Eight episodes of ventilation were in children who were admitted more than once during the study period.

Four children were excluded, two had tracheostomies, one was admitted intubated for a tracheostomy and one was brain dead at admission.

Twenty-one (10.3%) of the children died during ventilation, two (1%) had a tracheostomy without a prior extubation, and two (1%) were transferred to another hospital prior to extubation. Seven children (3.4%) had ventilation withdrawn as part of a palliative care plan and an additional four had ventilation withdrawn after they had failed extubation at least once. One hundred and eighty four elective extubation episodes were analysed further.

The most common reason for admission to PICU was post cardiac surgical procedures; followed by respiratory disease (Table 1). Trauma constituted 6.5% of admissions, with 11 of 14 being traumatic brain injuries.

Comorbid conditions were common, with dysmorphism and a history of prematurity the most common (Table 1). Of the 34 children with documented

dysmorphology, 14 had Trisomy 21, five had foetal alcohol syndrome, two each had 22q deletion and VACTERL; one case each had CHARGE, VATER, Noonan syndrome, Alagille syndrome and Retts syndrome; and six patients were unclassified.

The median (IQR) duration of ventilation was 69.5 (22 – 149) hours, and the median duration of PICU stay was 6 (3 - 12) days. The mortality rate for all invasively ventilated admissions was 14.62%.

Twenty-one (11.4%) of the 184 elective extubations failed. Thirteen (61.9%) were female, and median age was 3.12 (IQR 0.89 – 11.68) months (table 1). The time to re-intubation was <24 hours in 15 (71.43%) cases, with seven (33.33%) re-intubations occurring <6 hours after extubation.

Table 1: Patient characteristics

Variables	All (n=216)	Failed extubation (n=21)	Successful extubation (n=163)	p
Age in months, median (IQR)	7.98 (1.58 – 44.39)	3.12 (0.89 – 11.68)	8.54 (2.04 - 40.54)	0.25
Male gender n (percentage)	104 (48.15)	8 (38.1)	81 (49.70)	0.34
Weight (Kg) median (IQR)	6.7 (3.3 – 13)	3.9 (2.5 – 18.5)	7.0 (3.5 – 13)	0.19
PIM3 score median (IQR)	0.03 (0.01 – 0.07)	0.04 (0.01 – 0.07)	0.02 (0.01 – 0.06)	0.13
Primary Diagnosis				
Cardiac surgery	58(26.9)	4 (19.05)	53 (32.52)	
Respiratory disease	43(19.9)	4 (19.05)	34 (20.86)	
Other surgery	23 (10.6)	4 (19.05)	18 (11.04)	
Sepsis and Septic shock	22 (10.2)	1 (4.76)	11 (6.75)	
Cardiac disease	20 (9.3)	5 (23.81)	11 (6.75)	
Neurologic disease	14 (6.5)	0	11 (6.75)	
Trauma	14 (6.5)	2 (9.52)	8 (4.91)	
Burns	6 (2.8)	0	6 (3.68)	
Transplant	4 (1.9)	0	4 (2.45)	
Other	12 (5.6)	1 (4.76)	7 (4.29)	
Comorbidities				
Prematurity	26 (12)	6 (28.57)	14 (8.59)	0.006
Genetic syndrome or dysmorphology	34 (15.74)	7 (33.33)	23 (14.11)	0.025
Chronic lung disease	5 (2.31)	2 (9.52)	2 (1.23)	0.047
HIV infection	7 (3.24)	0	5 (3.07)	0.416
HIV exposed	30 (13.89)	5 (23.81)	22 (13.50)	0.209

IQR, interquartile range; PIM3, paediatric index of mortality 3; HIV, Human immunodeficiency virus

Table 2: Peri-intubation factors assessed

Variables n (%)	All (n = 216)	Failed extubations (n = 21)	Successful extubations (n = 163)	p
NIV support prior to intubation	83 (38.4)	13 (61.9)	58 (35.6)	0.06
Emergency intubation	116 (53.7)	14 (66.7)	74 (45.4)	0.07
Primary Indication for Intubation				
Airway protection	6 (2.8)	0	5 (3.1)	0.66
Respiratory distress/failure	74 (34.3)	7 (33.33)	51 (31.3)	0.04
Cardiovascular instability	37 (17.1)	5 (23.81)	18 (11.0)	0.10
Neurology	33 (15.3)	3 (14.29)	20 (12.3)	0.80
Surgery and postop support	96 (44.4)	7 (33.33)	86 (52.8)	0.09
Place of intubation				0.31
Theatre	100 (46.3)	8 (38.1)	89 (54.5)	
PICU	40 (18.5)	5 (23.8)	26 (16.0)	
Another hospital	44 (20.4)	6 (28.6)	30 (18.4)	
Medical ER	17 (7.9)	0	8 (4.9)	
Ward	8 (3.7)	2 (9.5)	4 (2.5)	
Trauma ER	2 (0.9)	0	2 (1.2)	
Out of hospital	5 (2.3)	0	4 (2.5)	
Others				
Previous endotracheal intubation	72 (33.3)	8 (38.1)	56(34.4)	0.74
>Two attempts at intubation	22 (10.2)	3 (14.3)	18 (11.0)	0.54
Nasal intubation route	175 (81.0)	14 (66.7)	137 (84.0)	0.04
Cuffed ETT	134 (62.0)	11 (52.4)	105 (64.4)	0.27
Leak around the ETT at intubation	121 (56.0)	10 (47.6)	93 (57.1)	0.05
Complications during intubation	37 (17.1)	3 (14.3)	26 (16.0)	0.34
Re-intubation prior to planned extubation	37 (17.1)	4 (19.0)	25 (15.3)	0.69

Table 2: NIV, non-invasive ventilation; PICU, paediatric intensive care; ER, emergency room; ETT, endotracheal tube

Uncuffed ETTs were used 58.3% of neonates, 48.8% of all children less than 12 months old, and in 24.2% of those 12 months old and above. The ETT size used correlated with calculated sizes recommended in 53.8% (n=99), was bigger in 23.4% (n=43) and smaller in 22.8% (n=42). In 88.5% of the ETT that were bigger than the recommended size, cuffed tubes that correlated with the formula $(\text{age}/4) + 4$ were used instead of $(\text{age}/4) + 3.5$. This was most prevalent in children under five years of age (33.3%) whereas the use of ETT with smaller diameters than recommended was more prevalent in children above 10 years of age. There was no association between the disparity in size and stridor ($p=0.18$), extubation failure ($p=0.08$) or extubation failure secondary to upper airway obstruction ($p=0.24$). The route of intubation and whether or not the ETT was cuffed was not associated with extubation failure, $p = 0.51$ and $p = 0.22$ respectively.

Table 3: Peri-extubation factors assessed

Variables	All planned extubations (n = 184)	Failed extubations (n = 21)	Successful extubations (n = 163)	p
Steroid administered prior to extubation n (%)	63 (34.24)	11 (52.38)	52 (31.90)	0.06
Inotrope/vasopressor support at time of extubation n (%)	40 (21.7)	5 (23.8)	35 (21.5)	0.82
Neuromuscular blocking agent in preceding 24 hours n (%)	21 (11.4)	0 (0)	21 (12.9)	0.07
Decreased level of consciousness n (%)	32 (17.4)	9 (42.9)	23 (14.1)	0.001
Mode of ventilation n (%)				
Pressure control ventilation	136 (73.9)	16 (76.2)	120 (73.6)	0.19
Pressure support CPAP	47 (25.5)	5 (23.8)	42 (25.8)	0.97
Pressure support	1 (0.5)	0	1 (0.6)	0.17
Ventilator settings Median (IQR)				
FiO2	0.3 (0.25 – 0.32)	0.3 (0.21 – 0.33)	0.30 (0.25 – 0.30)	0.63
Peak inspiratory pressure (cmH2O)	15.0 (14.0 – 16.0)	15.0 (14.0 – 15.0)	15.0 (14.0 – 16.0)	0.80
Positive end expiratory pressure (cmH2O)	5 (5 – 5)	5.0 (5.0 – 5.0)	5.0 (5.0 -5.0)	0.22
Mean airway pressure (cmH2O)	9.0 (8.0 – 10.0)	8.0 (7.0 – 10.0)	9.0 (8.0 – 10.0)	0.60
Tidal volume (mls/kg)	6.4 (5.1 – 7.9)	5.7 (5.0 – 7.0)	6.5 (5.2 – 8.0)	0.075
Duration of ventilation prior to 1 st extubation (hrs.)	57.6 (22 – 123)	112 (50 – 174)	49 (21 – 116)	0.012

CPAP, continuous positive airway pressure; IQR, interquartile range

Table 4: Pre-extubation assessment

Variables	All planned extubations (n = 184)	Failed extubations (n = 21)	Successful extubations (n = 163)	p
Blood gas analysis done n (%)	174 (94.6)	21 (100)	153 (93.9)	
pH	7.39 (7.34 – 7.43)	7.39 (7.37-7.43)	7.44 (7.38 – 7.45)	0.51
PCO ₂ (kPa)	5.53 (4.88 – 6.28)	6.23 (5.22 – 6.9)	5.5 (5.3 – 5.6)	0.09
PO ₂ (kPa)	13.10 (8.91 – 17.60)	9.23 (6.05 – 11.2)	18.7 (11.0 – 20.6)	0.21
Base excess	-0.01 (-3.75 – 4.3)	4.4 (2.0 – 6.5)	4.3 (3.7 – 4.8)	0.22
Bicarbonate (mmol/L)	24.2 (21.2 – 27.7)	27.8 (25.7 – 29.2)	27.9 (27.7 – 29.2)	0.23
Cumulative fluid balance (% of body weight)	1.87 (0.12 – 7.01)	6.33 (1.12 – 9.12)	1.68 (0.11- 6.32)	0.10
Haemoglobin level (g/dL)	11.0 (9.4 – 12.7)	11.1 (10.0 – 12.6)	11.0 (9.4 – 12.7)	0.75
Transfused prior to extubation n (%)	56 (30.4)	5 (23.8)	51 (31.3)	0.45
Documented leak around ETT at extubation n (%)	123 (66.9)	15 (71.4)	108 (66.3)	0.88
Impaired level of consciousness	32 (17.4)	9 (42.9)	23 (14.1)	0.001

Table 5: Non-invasive ventilation post extubation

Ventilatory support post extubation n (%)	All planned extubations (n = 184)	Failed extubations (n = 21)	Successful extubations (n = 163)	p
Total number provided NIV post extubation	98 (52.3)	16 (76.2)	82(50.3)	0.025
NIV started immediately after extubation	57 (40.0)	11 (52.4)	46 (28.2)	<0.0001
HFNC	30 (16.3)	7 (33.3)	23 (14.1)	
CPAP	63 (34.2)	7 (33.3)	56 (3)	
BiPAP	5 (2.7)	2 (9.5)	3 (1.8)	

Tables 4 and 5

PCO₂, partial pressure of carbon dioxide; PO₂, partial pressure of oxygen; NIV, non-invasive ventilation; HFNC, high flow nasal cannula; CPAP, continuous positive airway pressure; BiPAP, bi-level positive airway pressure.

On univariate analysis prematurity, dysmorphology, decreased level of consciousness, ventilation ≥ 48 Hours, oral intubation route and the use of NIV were associated with extubation failure. On multiple regression analysis, dysmorphology ($p = 0.006$), prematurity ($p = 0.007$), decreased level of consciousness ($p = 0.001$), and ventilation ≥ 48 hours ($p = 0.016$) were found to be independent predictors of extubation failure.

Table 6: Outcomes of failed extubation

Variable	All planned extubations (n = 184)	Failed extubation (n = 21)	Successful extubation (n = 163)	p
Duration of mechanical ventilation (hours) median (IQR)	69.5 (22 – 149)	231.0 (146.0 – 341.0)	53 (21.67 – 123.0)	<0.0001
Stridor present post extubation n (%)	47(25.5)	8 (38.1)	39 (23.9)	0.358
Complications of invasive ventilation n (%)	58 (31.5)	12 (57.1)	46 (28.2)	0.027
PICU LOS Median (IQR)	6 (3 – 12)	15.0 (9.0 – 20.0)	5 (2.0 – 9.0)	<0.0001
PICU mortality; n (%)	4 (2.2)	2 (9.5)	2 (1.2)	0.014
Mortality 30 days post PICU discharge n (%)	17 (9.2)	6 (28.6)	11 (6.7)	0.001
Hospital LOS (of survivors) Median (IQR)	16 (8 – 28)	32 (21 – 53)	15 (8 – 27)	0.009

IQR, interquartile range; PICU, paediatric intensive care unit; LOS, length of stay

Complications of invasive mechanical ventilation

There were 89 documented complications in 58 (26.9%) of the children, most commonly sepsis and ventilator associated pneumonia (Figure 1). Twenty-one (9.7%) of the children died prior to extubation.

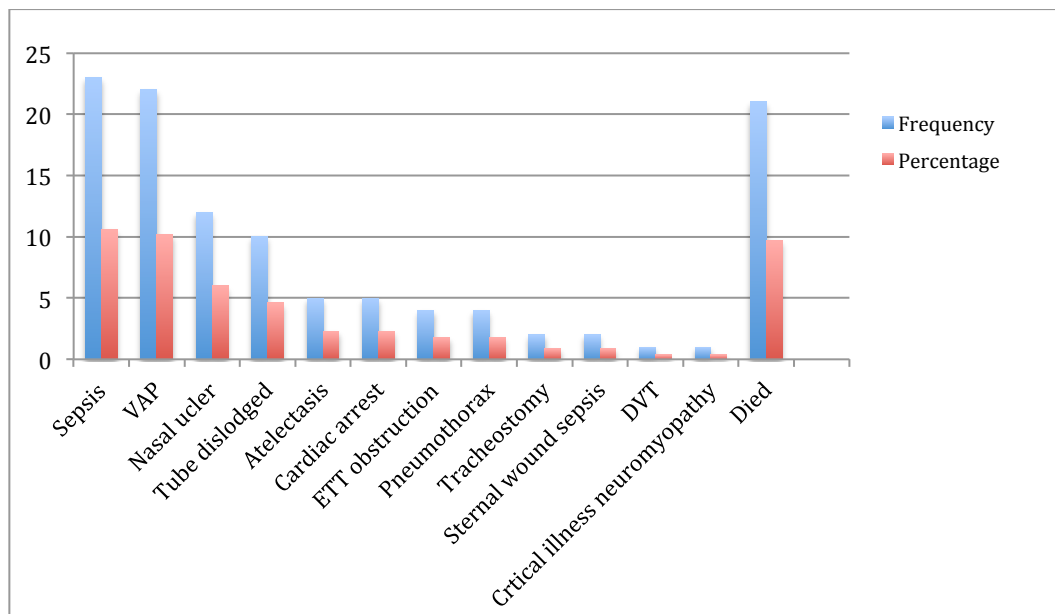


Figure 1: Complications associated with invasive mechanical ventilation

At the time of extubation, 41 (22.3%) of the children were on inotropes or vasopressors. Milrinone was predominant, 15.8% at a dose of between 0.5 and 0.75 mcg/kg/min. Adrenaline was the second commonest, 13.6%, running at doses of between 0.02 and 0.06 mcg/kg/min. Fifteen (8.2%) were on both adrenaline and milrinone. None of them were on dopamine or dobutamine. The use of inotropes and vasopressors at the time of extubation did not affect the outcome ($p = 0.82$).

Eighty-four (45.65%) children were on morphine, 10 (5.4%) on fentanyl, 5 (2.72%) on dexmedetomidine and 1 (0.5%) each on ketamine or midazolam at the time of extubation.

Sixty-four (34.78%) children received steroids prior to extubation, 19 of whom where for indications other than upper airway oedema. These included post-solid organ transplant immunomodulation (n=6), hypotension (n=4) and TB meningitis (n=3). Dexamethasone was used for upper airway oedema, methylprednisolone or prednisolone for transplant immunomodulation and hydrocortisone for hypotension. The median duration from time of the first dose to time of extubation was five and a half hours in the extubation failure group and 23.5 hours in the successful extubation group.

Stridor occurred in 47 (25.54%) children of whom 18 (38.30%) had received at least one dose of a steroid prior to extubation. The use of steroids did not result in decreased stridor ($p = 0.6$). The use of a cuffed ETT ($p = 0.24$) and replacement of the ETT prior to planned extubation was not associated with stridor ($p = 0.15$). However, the use of orally placed ET tubes ($p = 0.008$) and two or more attempts at intubation ($p = 0.001$) were associated with stridor. The presence or absence of a leak around the ETT prior to extubation was only documented in 142 (77.17%) of the extubations. Of the 47 children that developed stridor, 25 (53.19%) had a leak, 8 (17.02%) had no leak around the ETT and 14 (29.79%) had no documentation of whether or not there was a leak. Eight (42.11%) of the total of 19 patients that did not have a leak developed stridor when extubated ($p = 0.19$). Stridor was not associated with extubation failure ($p = 0.37$).

A cumulative fluid balance $\geq 10\%$ body weight occurred in 14.7% (n=27) at the time of extubation and in 23.8% (n=5) of children who failed extubation ($p=0.23$). This was however not associated with extubation failure even when those with upper airway obstruction were excluded ($p=0.47$)

Ninety-eight (52.26%) of the children were placed on NIV after extubation, 57 started electively immediately after extubation and 41 later when it was deemed necessary. Of the 57 children that received NIV immediately after extubation, 11 (19.29%) were re-intubated compared with 5 out of 41 children (12.20%) for those who received NIV non-electively. Complications occurred in three children (3.10%). One developed a pneumothorax and two had pressure ulceration of the nasal septum both of which were mild.

Upper airway obstruction (n=7; 33.33%) was the most common indication for re-intubation within 48 hours of planned extubation, followed by respiratory distress or failure (n=4; 19.05%), heart failure (n=3; 14.29%); hypoventilation, diaphragm paralysis and cardiac arrest (n=2; 9.52% each), and decreased level of consciousness (n=1). The causes of upper airway obstruction were laryngeal oedema (n=4), vocal cord paralysis (n=2), and laryngeal web (n=1).

Of the 21 children who failed extubation, two died and one was transferred to another hospital intubated. An upper airway endoscopy was carried out for three of them. The findings were laryngeal web (congenital), vocal cord paralysis (following severe traumatic brain injury) and laryngeal injury (from intubation). Two got tracheostomies and sixteen were extubated. Eleven out of the 16 (68.8%) received steroids prior to their second extubation. Three (18.8%) of them failed their second extubation and one failed a third extubation. The median duration of re-intubation was 126 hours (IQR 60.5 – 190 hours).

Extubation failure was associated with increased total duration of invasive mechanical ventilation ($p < 0.0001$), increased PICU length of stay ($p < 0.001$) and hospital stay ($p = 0.009$) as well as higher PICU mortality ($p = 0.014$) and higher mortality at 30 days post PICU discharge ($p = 0.001$) (Table 6).

Discussion

We report an invasive ventilation rate of 48.4%; median duration of ventilation of 69.5 hours and median PICU stay of six days, which is comparable to data from other PICUs (2, 3, 26).

Our extubation failure rate at 48 hours was 11.4%. Most reports on failure rates in children range between 4 – 20% (8, 9, 14, 17, 27-30). There is no recommended or acceptable extubation failure rate. It is suggested that very low extubation failure rates may indicate overly conservative weaning and extubation practices. Siddhartha et al related ventilator-free days, ICU-free days and mortality to the extubation failure rates in their ICU over a 9-year period and found that periods of extubation failure rate between 7 – 15% had higher ventilator and ICU-free days compared with failure rates of < 7% or >15%, with no significant difference in mortality. This was however a study in adults and may not be generalizable to children.

The factors we found to be associated with extubation failure are similar to those reported in other studies: prematurity or a history of prematurity in infants, dysmorphology, duration of ventilation \geq 48 hours, and a decreased level of alertness (6, 8, 27, 28, 31). Prematurity was an important risk factor in our PICU because it also serves newborns requiring surgical interventions in our catchment area.

Though some studies have shown increased morbidity with blood transfusion and fluid overload, this was not evident in our results (32-34). This maybe because sub group analysis was not carried out due to the small population size. There is a conscious effort to prevent fluid overload in our ICU, including the use of diuresis. In addition, the fluid balance reported in this study was at the time of extubation and not necessarily during the acute phase of the first 24 - 48 hours described in most of the PICU fluid overload outcome studies, and excluded

those that died prior to extubation (35-39). Randolph et al in a multicenter study of 301 mechanically ventilated children also found that fluid balance at the time of extubation was not a predictor of extubation outcome (40).

Upper airway obstruction was the major reason for re-intubation in a third of failed extubations. This is also consistent with findings from other studies (6, 7). Respiratory distress or failure, heart failure, hypoventilation, and diaphragmatic dysfunction together were the indications for re-intubation in 11 (52.38%) of the children. There may therefore be a role for formal SBT for children at higher risk such as those with cardiac disease, residual neurologic or neuromuscular impairment, infants with a history of prematurity, those ventilated for > 48 hours and those with genetic syndromes or dysmorphology since these were identified as risk factors for extubation failure. It is recommended that point of care ultrasound scans be explored to better assess cardiac and diaphragmatic function in high-risk patients to aid in assessing extubation readiness (41-44).

The prophylactic use of corticosteroids for the prevention of post extubation stridor and extubation failure remains controversial. In a randomized double blinded study by Tellez et al at the Children's Hospital of Los Angeles, the prophylactic use of corticosteroids did not significantly decrease the incidence of post extubation stridor or re-intubation (45). A meta-analysis by Markovitz et al of six randomised controlled trials examining the use of corticosteroids for the prevention of re-intubation and post-extubation stridor in neonates and paediatric patients also showed a reduction in stridor but no significant trend toward a decreased rate of re-intubation when prophylactic steroids were used (46). Another meta-analysis by Khemani et al of studies involving neonates, children and adults also showed a general nonsignificant decrease in stridor and extubation failure in the study that excluded children with airway abnormalities but a significant reduction in the incidence of post extubation stridor and extubation failure in the study who's population included children with underlying airway abnormalities (47). This suggests that targeted use in those at risk of UAO

is beneficial. Studies in adults have show decrease in post extubation stridor when steroids are started 12-24 hours prior to extubation compared with a single dose (48, 49).

During our study, dexamethasone was administered at variable times prior to extubation to those assessed to be at high risk of upper airway obstruction. These generally were children who had multiple attempts at intubation, prolonged intubation or pre-existing concerns about upper airway compromise or the absence of a leak around the endotracheal tube. Of the 63 children that received steroids, 18 (28.6%) developed stridor, and 11 (17.5%) failed extubation. The median time from administration of the steroid to extubation was 5.5 hours in the extubation failure group compared to 23.5 hours in those who did not fail. Timing may therefore not have been optimal. More studies will have to be conducted to provide clearer guidelines as to the dose and duration of dexamethasone prior to extubation.

Non- invasive ventilation (NIV) is being increasingly employed to facilitate earlier extubation across different disciplines (9, 22, 50-53). Its use after extubation was therefore not considered as extubation failure. The re-intubation rate was higher among those started on NIV immediately after extubation (19.3% versus 12.2%) compared to those started later in our study. This was the reverse to findings by Mayordomo-Colunga and colleagues study that showed better outcomes in those who received NIV electively (23).

Extubation failure was associated with increased duration of ventilation, increased adverse events during ventilation and longer PICU stay, and higher mortality, which is consistent with many other studies (6-9, 54).

Adverse events occurred in 31.5% of the children who underwent invasive mechanical ventilation, the commonest being infection related complications. There was a high incidence of ETT dislodgement or accidental extubation, 4.6%

n=10. They all occurred in children less than five years, 2 in neonates, 6 in children under one year and 2 in those below five years. Unlike in other reports where re-intubation rates were 16 – 65%, all 10 were re-intubated (1, 55). The adverse event rates are high and present an opportunity for quality improvement programs to reduce the rate of adverse events and optimize patient outcome

Study limitations

This was a study in a single centre that admits children from newborn to 13 years of age, which limits generalizability. In addition, the study was over a 4-month period that included the local winter flu season that may have introduced bias. The number of extubations analysed and the number of failed extubations also limits the power to draw firm conclusions. The use of the AVPU scale to classify the level of consciousness of the patients left room for wide intra group variations.

Conclusions

Dysmorphology, prematurity, decreased level of consciousness, and ventilation for 48 hours or more, are independent predictors of extubation failure in our setting. Extubation failure is associated with longer duration of ventilation, longer PICU and hospital stay and a four-fold increase in mortality. The identification of the major factors associated with extubation failure affords us the opportunity to re-evaluate our extubation readiness assessment criteria in these sub-populations to reduce our failure rate. Although this study does not add new information to what has already been described in other studies over the years, it provides a basis for future more extensive collaborated studies and data for quality improvement.

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Appendices

1.1 Appendix 1: Data collection form

Demography

1. Study number
2. Hospital Number
3. Name
4. Date of birth
5. Date of PICU admission:
6. Date of PICU discharge:
7. Convalescent Weight: Z score
8. Gender 1. Male ☐ 2. Female ☐
9. Primary discharge diagnosis:.....
10. Secondary diagnosis
 1. HIV infection ☐ 2. HIV exposed but PCR neg. ☐ 3. Airway abnormality ☐.....
 4. Genetic syndrome or Dysmorphic ☐.....
 5. Prematurity ☐ 6. Neurologic disease ☐
 7. Neuromuscular disease ☐8. Congenital Cardiac disease ☐
 9. Heart failure of other cause ☐.....10. Lower respiratory tract infection ☐
 11. Chronic lung disease ☐12. Other organ impairment ☐
 -12.Other.....
11. PIM III score
12. Previous endotracheal intubation? 1. Yes ☐ 2. No ☐
13. Use of NIV prior to intubation 1. CPAP ☐ 2. HFNC ☐ 3. BIPAP ☐
4. None ☐

Intubation

14. Date of intubation: Time:.....
15. 1. Elective intubation ☐ 2. Emergency intubation ☐
16. Indication for intubation
 1. Airway protection ☐ 2. Respiratory failure ☐
 3. Cardiovascular instability ☐ 4. Neurological problem ☐
 5. Surgery & Postoperative support ☐
17. Where was the intubation carried out?
 1. PICU ☐ 2. Theatre ☐ 3. ER ☐ 4. Trauma ER ☐
 5. Ward ☐ 6. Another hospital ☐ 7. Out of hospital ☐
18. Number of attempts at intubation..... Unknown ☐

19. ETT size
20. Nasal or oral tube? 1. Nasal ☐ 2. Oral ☐
21. 1. Cuffed tube ☐ 2. Uncuffed tube ☐
22. Was there a leak around the ETT? 1. Yes ☐ 2. No ☐
23. Complications during intubation:
1. None ☐ 2. Trauma ☐ 3. Vomiting or aspiration ☐
4. Hypotension ☐ 5. Desaturation (<85% 0r < 60% if cyanotic heart dx) ☐
6. Bradycardia ☐ 7. Cardiac arrest ☐ 8. Data not available ☐
9. Other ☐
24. How many times was the ETT replaced in the PICU prior to planned extubation and why?

Ventilation

25. Mode of ventilation prior to extubation
1. Pressure control (PC) ☐ 2. Volume control (VC) ☐ 3. HFOV (oscillation) ☐
4. Pressure regulated volume control (PRVC) ☐
4. Pressure support CPAP (PSCAP) ☐ 5. Pressure support (PS) ☐
6. Other ☐
26. FiO2 prior to extubation
27. PIP prior to extubation.....cmH₂O.
28. PEEP prior to extubation..... OR Amplitude if on HFOV
29. Mean airway pressurecmH₂O.
30. Tidal volume..... mls/kg
31. A. Set respiratory rate OR Frequency if on HFOVB. Actual rate/min.

Drugs

32. Were steroids administered prior to extubation? 1. Yes ☐ 2. No ☐
33. If yes, how long before extubation?hours.
34. Number of doses of administered pre-extubation:
35. Steroid administered? 1. Dexamethasone ☐ 2. Prednisone ☐
3. Hydrocortisone ☐ 4. Methyl prednisone ☐
36. Was there a reason for steroids besides airway oedema?
37. Was the child on inotropes or vasopressors at the time of extubation?
1. Yes ☐ 2. No ☐
38. If yes, indicate drug and dose:.....
39. Sedatives administered in the preceding 24 hours. Please state dose.
1. Morphine ☐ 2. Midazolam ☐
3. Clonidine ☐ 4. Diazepam (valium) ☐
5. Dexmedetomidine (precedex) ☐ 6. Ketamine ☐
7. Other ☐

40. Time of last dose of sedatives prior to extubation (hrs.)

.....
.....

41. Sedative infusions running at time of extubation and dose:

1.....

2. 3. Nil ☐

42. Were any neuromuscular blockers administered in the preceding 24 hours?

1. Yes ☐ 2. No ☐

43. If yes, how many hours prior to extubation was the last dose given?

.....

44. Pre Extubation ABG or VBG result: 1. ABG ☐ 2. VBG ☐ 3. No blood gas done ☐

pH..... pCO₂ pO₂ BE HCO₃

Lactate

45. Complications of invasive ventilation

1. None ☐ 2. VAP ☐ 3. Nasal necrosis ☐ 4. Pneumothorax ☐

5. Accidental extubation ☐ 6. Tracheostomy for prolonged ventilation ☐

7. Other ☐

46. Cumulative fluid balance mls/kg

47. Haemoglobin levelg/dL . Transfused in PICU? 1. Yes ☐ 2. No ☐

Extubation

48. Date of Extubation: Time:.....

49. Coma score at time of extubation(circle appropriate score) : A V P U

50. Was there a leak around the ETT? 1. Yes ☐ 2. No ☐ 3. Don't know ☐

51. Extubated to: 1. Room air ☐ 2. NPO₂ ☐ 3. HFNC ☐

4. CPAP ☐ 5. BIPAP ☐

52. Was there stridor post extubation? 1. Yes ☐ 2. No ☐

53. Where steroids administered post extubation? 1. Yes ☐ 2. No ☐

54. Were adrenaline nebs administered post extubation? 1. Yes ☐ 2. No ☐

Non-invasive ventilation (NIV) use

55. Was NIV provided post extubation? 1. Yes ☐ 2. No ☐

If no NIV used then move to number 62

56. How soon was it started? 1. Immediately after extubation ☐ 2.....hrs. later ☐

57. What NIV support was used?

1. CPAP ☐ 2. BIPAP ☐ 3. HFNC (Airvo) ☐ 4. HFNC (BCPAP circuit) ☐

58. PEEP/CPAP..... Flow..... L/min FiO₂%

59. Was there a switch from one form of NIV to the other?

1. Yes ☐ Fromto afterdays/ hours.

2. No ☐

60. What was the total duration of NIV?hours

61. Complications of NIV

1. None ☐ 2. Nasal necrosis ☐ 3. Failed NIV (intubated) ☐
4. Other ☐

Reintubation

62. Was he/she re-intubated? 1. Yes ☐ 2. No ☐

If not re-intubated then move on to number 70

63. How long after extubation was he/she re- intubated? hours.

64. What was the indication?

1. Upper airway obstruction ☐ 3. Diaphragm dysfunction ☐
2. Respiratory failure 2.1. Hypoxia ☐ 2.2 Hypercarbia ☐
4. Worsening heart failure ☐ 5. Decreased level of consciousness ☐

65. Pre intubation ABG or VBG result: 1. ABG ☐ 2. VBG ☐ 3. No blood gas done ☐
pH..... pCO₂ pO₂ BE HCO₃ Lactate

66. If re-intubated for upper airway obstruction, what was the cause?

1. Laryngeal oedema ☐ 2. Vocal cord paralysis ☐
4. Not documented ☐ 3. Other ☐

67. What was the duration of re-intubation before successful extubation?.....hours

68. Total number of failed extubations?

1. 1 ☐ 2. 2 ☐ 3. >= 3 ☐ 4. None ☐

69. Complications of invasive ventilation post failed extubation

1. None ☐ 2. VAP ☐ 4. Nasal necrosis ☐ 5. Pneumothorax ☐
6. Post extubation stridor ☐ 7. Accidental extubation ☐
8. Tracheostomy for prolonged ventilation ☐ 9. Other ☐

70. Total duration of intubation and mechanical ventilation prior to successful extubation hours

71. Ventilatory support at time of PICU discharge:

1. None ☐ 2. NPO₂ ☐ 3. CPAP ☐ 4. BiPAP ☐ 5. HFNC ☐
6. Tracheostomy and continued mechanical ventilation ☐
7. Tracheostomy but not ventilated ☐
8. Transferred to another hospital still intubated and ventilated ☐

72. PICU death? 1. Yes ☐ 2. No ☐

73. Outcome 30 days post PICU discharge

1. Discharged home ☐ 2. Transferred to another hospital ☐
3. Still on admission on ward ☐ 4. Readmitted to PICU ☐ 5. Died ☐

74. Date of hospital discharge:

1.2 Appendix 2: Report on Endotracheal intubation

1.1 Patient details:

Place patient sticker in this area

1.2 Time and place:

h

Site of intubation:

1.3 Operator

Name:

1.4 Drugs used:

Agent	Dose	Route
Agent	Dose	Route
Agent	Dose	Route
Agent	Dose	Route

1.5 Endotracheal tube

Route: oral / nasal / oral then nasal

Cuff?

Y /N

Size (mm):

Length at cords (cm):

Length at lips / nose (delete whichever is appropriate):

Is there a leak present?

Y /N

1.6 Procedure:

1.6.1 Number of attempts:

View of the larynx: complete (circle appropriate grade)

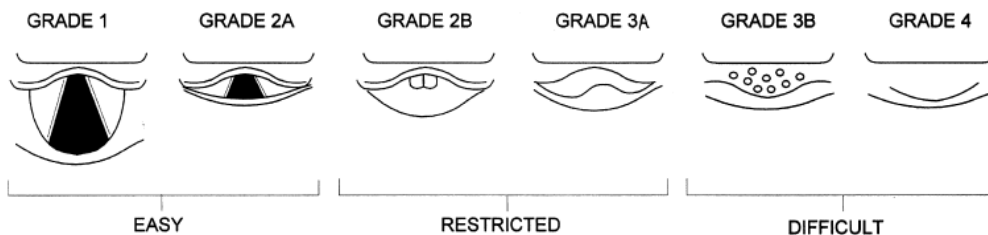




Figure 1 Cormack and Lehane classification and new classification of view at laryngoscopy.

1.6.2 Complications (please specify under the following headings)

Trauma:	Y /N
Vomiting or aspiration	Y /N
Desaturation (saturation <85% at any stage during the procedure)	Y /N
Hypotension	Y /N
Bradycardia	Y /N
Cardiac arrest	Y /N
Other (comment on any specific difficulty with the procedure):	

1.3 Appendix 3: Human Research Ethics Committee, University of Cape Town

	UNIVERSITY OF CAPE TOWN Faculty of Health Sciences Human Research Ethics Committee	
		<small>Room E53-46 Old Main Building Groote Schuur Hospital Observatory 7925 Telephone [021] 406 6626 Email: shuretta.thomas@uct.ac.za Website: www.health.uct.ac.za/fhs/research/humanethics/forms</small>

18 April 2017

HREC REF: 166/2017

Dr Shamiel Salie
Paediatric and Child Health, PICU
Red Cross War Memorial Children's Hospital

Dear Dr Salie

PROJECT TITLE: PERIEXTUBATION PRACTICES AND EXTUBATION FAILURE IN CHILDREN ADMITTED TO THE PAEDIATRIC INTENSIVE CARE UNIT OF THE RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL (MPhil-candidate-M Kilba)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 April 2018.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)


Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate Institutional approval before the research may occur.

The HREC acknowledges that the student, M Kilba will also be involved in this study.

Please quote the HREC reference number in all your correspondence.

Yours sincerely



PROFESSOR M. BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.

Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical

Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines.

The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code of Federal Regulation Part 312.61, 312.62 and 312.63.

1.4 Appendix 4: Approval from Red Cross War Memorial Children's Hospital for the study



Dr Jane Kawadza
Manager: Medical Services
Email: Jane.Kawadza@Westerncape.gov.za
Tel: +27 21 658 5788 fax: +27 21 658 5166
RXH: RCC71

Dr C Kilba
Red Cross War Memorial Children's Hospital

Dear Dr C Kilba

APPROVAL OF RESEARCH

PROJECT TITLE: PERIEXTUBATION PRACTICES AND EXTUBATION FAILURE IN CHILDREN ADMITTED TO THE PAEDIATRIC INTENSIVE CARE UNIT OF THE RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL

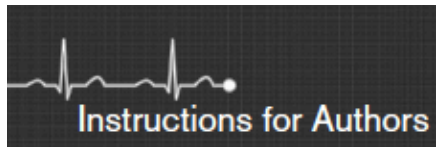
It is a pleasure to inform you that approval is hereby granted to conduct the above-mentioned study at Red Cross War Memorial Children's Hospital.

Yours sincerely,

A handwritten signature in black ink, appearing to be "J. Kawadza", written over a horizontal line.

Dr J Kawadza
Manager: Medical Services
Date: 05.05.17

1.5 Appendix 5: Pediatric Critical Care Medicine Journal author guidelines



Pediatric Critical Care Medicine is an international, peer-reviewed journal that is interested in publishing the highest quality scientific studies in the field of pediatric critical care medicine.

MANUSCRIPT SUBMISSION

Manuscripts are submitted through Editorial Manager®, a Web-based manuscript tracking system in use by SCCM. This system allows authors to add a new manuscript or check the status of a submitted manuscript, while shortening the time needed for processing manuscripts in the Editorial Office and through peer review. To submit manuscripts for consideration, go to www.sccm.org, choose *Pediatric Critical Care Medicine* under the Publications tab, then select "Submit Manuscripts." Once you reach the Editorial Manager® home page, log on to the system by creating an account or entering through your existing account.

Editorial Manager® will easily guide authors through the manuscript submission process. Required information pertaining to the manuscript includes the name, address, telephone number, and e-mail address for the first author and all contributing authors; affiliated institutions; title of the manuscript; abstract; and key words. If authors wish, they may provide optional information that includes author's suggested reviewers and author's nonpreferred reviewers. The Editorial Office will automatically be notified of the submission and will send an e-mail confirming the submission of the manuscript to the author(s). After editorial office review of the submitted documents, a manuscript number will be assigned to each submitted manuscript, which will be used in all correspondence.

Each manuscript submission should designate one corresponding author and all contributing authors. The number of authors should be restricted to only those persons who have truly participated in the conception, design, execution, and writing of the manuscript. Authors must disclose any potential financial or ethical conflicts of interest regarding the contents of the submission.

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Conflicts of Interest and Source of Funding: "Author A" has received honoraria from "Company I." "Author B" is currently receiving a grant (#12345) from "Organization Y," and is on the speaker's bureau for "Organization X" – the CME organizers for Company I. For the remaining authors none were declared.

Human and Animal Subjects. All studies of human subjects must contain a statement within the Materials and Methods section

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Standard Book with Editors: Norman LJ, Reforn SJ (Eds): *Mental Health Care for Elderly People*. New York, Churchill Livingstone, 1996

Standard Chapter in a Book: Phillips SJ, Whisnant JP: Hypertension and stroke. In: *Hypertension: Pathophysiology, Diagnosis and Management*. Laragh JH, Brenner BM (Eds). Second Edition. New York, Raven Press, 1995, pp 465-478

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